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## Cost-Effectiveness Analysis of CT Colonography for Colorectal Cancer Screening Program to Working Age in Japan

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### ABSTRACT

**Objectives:** To assess the cost-effectiveness of computed tomography colonography (CTC) for a colorectal cancer screening program in a working population (aged 40–60 years) from a health care payer's perspective in Japan. **Methods:** A Markov model for colorectal cancer was constructed to estimate the long-term (10-year, 20-year, and 30-year) effect of introducing CTC for three different strategies in the cohort aged 40 years on April 1, 2011. Strategy 1 (the current strategy in Japan): fecal occult blood test (FOBT) followed by optical colonoscopy (OC). In this case, 41.8% of those who were FOBT-positive did not undergo OC (uptake 58.2%). Strategy 2: All FOBT-positive cases would be offered CTC (uptake 79.1%) followed by OC. Strategy 3: Only those FOBT-positive cases who were reluctant to undergo OC (41.8%) would be offered CTC (assumed uptake 50.0%) followed by OC. Epidemiological data were obtained mainly from statistics published by the Japanese National Cancer Center. We set quality-adjusted life-year (QALY) as the primary outcome and colorectal cancer death and expected life-years as secondary ones. The discount rate for both costs

and outcomes was set at 3%. **Results:** In the base-case (20-year) analysis, total cost was increased from Japanese yen (JPY) 65,614 million (strategy 1) to JPY 69,405 million (strategy 2) but was decreased to JPY 63,878 million (strategy 3). The total QALY increased from 28,156,046 QALYs (strategy 1) to 28,158,349 (strategy 2) and 28,159,058 QALYs (strategy 3). Therefore, the incremental cost-effectiveness ratio was JPY 1,646,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1, both of which were well below the Japanese threshold (JPY 5–6 million per QALY gained). **Conclusion:** Adding CTC into the current colorectal cancer screening program for the working population seems to be a cost-effective option.

**Keywords:** colorectal cancer, cost-effectiveness analysis, computed tomography colonography (CTC), Japan, Markov model.

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### Introduction

#### Epidemiology of Colorectal Cancer in Japan

The 5-year observed survival rates of colorectal cancer in the member hospitals of the Association of Clinical Cancer Centers (diagnosed in 2000–2004) were 89% for stage 1, 80% for stage 2, 67% for stage 3, and 15% for stage 4 [1]; therefore, if patients with stage 4 colorectal cancer were diagnosed at an earlier stage, deaths from colorectal cancer would be expected to decrease dramatically. In reality, however, the incidence rate and mortality of colorectal cancer have been increasing year by year, with colorectal cancer being the most common and the third most common cause of cancer-related death in women (30.8/100,000 persons) and men (37.4/100,000 persons), respectively [2,3]. Furthermore, according to the report titled “Estimates of National Medical Care Expenditures 2010,” colorectal cancer consumed Japanese yen (JPY) 499.8 billion (US \$1 = JPY 85) in 2010, which was the biggest among all cancers [4].

#### Current Situation and Issues Regarding Colorectal Cancer Screening in Japan

##### Current colorectal cancer screening situation

Currently, cancer screening is available for only five sites: the stomach, uterine cervix, breasts, lungs, and colon [5,6]. In Japan, people older than 40 years were recommended to undergo fecal occult blood test (FOBT) annually, followed by optical colonoscopy (OC) in those who were FOBT-positive [6]. The Basic Plan to Promote Cancer Control Program, which was set on the basis of the Cancer Control Act 2006, aims to raise the uptake in each cancer screening program to 50% [7]. As a means of early detection and reducing mortality, colorectal cancer screening by FOBT and OC, with relevant interventions, has been shown to be effective in the research project funded by the Ministry of Health, Welfare and Labor [8]. Improvement in the colorectal cancer screening uptake may be linked to reducing the incidence rate and mortality.

The uptake of colorectal cancer screening for working age people, or between 40 and 60 years, in Japan was only 24.8% in

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2010 [9,10], which was as low as a half of the government's target figure (50%). Moreover, about 40% of those who were FOBT-positive did not undergo OC for various reasons [10,11]. Although some already had colorectal cancer, it would not be detected until a later stage.

The major reasons why people avoid screening were as follows: "inconvenient," "too busy to go to hospital," and "no screening institution local to me." There was also insufficient understanding about the test, for example, "reluctant to undergo a painful test" and "unfamiliar with the test" [11].

#### *Future policies and expected issues*

In an attempt to increase the uptake of colorectal cancer screening to 50% among the working age population, the government has provided FOBT test kits free to those who become 40, 45, 50, 55, or 60 years old since 2011 [11].

Under the assumption that the uptake of the tests was unaffected by subjects' colorectal cancer status, if the uptake of FOBT reached 50% and all subjects who were FOBT-positive agreed to OC, 64,466 patients with colorectal cancer would be detected [10]. If the OC screening uptake remained at its current level (58.2%), however, 26,560 of the 64,466 patients with colorectal cancer would not be identified. The uptake of FOBT and OC is crucial for both increasing the number of early detected patients and to reduce the number of colorectal cancer deaths.

#### *Computed tomography colonography*

Computed tomography colonography (CTC) is a noninvasive testing method that diagnoses colorectal cancer by dilating the colon with gas and taking a three-dimensional image of the colon using an advanced multislice computed tomography scanner [12]. CTC is less invasive and requires a shorter time for diagnosis than does conventional OC. Therefore, it is expected to improve the uptake of colorectal cancer screening. CTC is widely used as a colorectal cancer screening method in Europe and the United States. For example, according to the guideline for cancer screening dispatched by the American Cancer Society in 2008, CTC is recommended every 5 years for detecting adenomatous polyps and cancers [13,14]. In Japan, it has been used mainly as a preoperative diagnostic method for colorectal cancer. The National Cancer Center of Japan began CTC-based colorectal cancer screening in November 2010 [12], and this drew attention to CTC as a screening method. CTC-based colorectal cancer screening is expected to expand in the future.

#### *Economic Evaluations of CTC for Colorectal Cancer Screening (Literature Review)*

Economic evaluations of CTC in colorectal cancer screening have already been carried out in the United Kingdom [15,16]. Both studies chose the same target population (people aged 60–69 years), the same control (current colorectal cancer screening program in the United Kingdom), and the same perspective (UK National Health Service). In the United Kingdom, individuals aged 60 to 69 years were offered FOBT every 2 years, followed by OC in those who were FOBT-positive [15–17].

Lee et al. [15] found that adding CTC to the existing program as a secondary screening program to triage FOBT-positive patients was less costly than OC, but increased the number of deaths from colorectal cancer by 2 people for every 100,000 cases over 10 years. In contrast, using CTC as a primary screening program every 5 years was more expensive than biennial FOBT screening but resulted in fewer deaths.

Sweet et al. [16] found that CTC screening offered every 10 years was cost saving compared with the current UK program of biennial FOBT screening followed by OC. In addition, this strategy

yielded greater health benefits (quality-adjusted life-years [QALYs] and life-years) than did biennial FOBT screening. The authors suggested, however, that the generalizability of their results from the UK setting to other countries may not be appropriate in light of the difference in cost setting, approaches to using OC in screening, or the age range of the target population.

In Japan, there has been no economic analysis of CTC for the colorectal cancer screening program; however, under the situation that using CTC as a cancer screening method would improve cost-effectiveness, decision makers needed a study that reveals an improvement in outcomes and an increase in cost as a result of introducing CTC as a cancer screening method.

#### **Objective**

In this study, we aimed to assess the cost-effectiveness of CTC for the colorectal cancer screening program for the working age population in Japan. We conducted a cost-effectiveness analysis of CTC introduction, including its long-term effect, in people aged 40 years on April 1, 2011, from a health care payer's perspective. We set QALY as the primary outcome and colorectal cancer death and expected life-years as secondary ones.

#### **Methods**

##### *How to Introduce CTC Into the Japanese Colorectal Cancer Screening Program*

We designed the following three colorectal cancer screening strategies for this study. These strategies are illustrated in Figure 1. In the explanation below, the numbers in parentheses indicate the average uptake among people aged 40 to 60 years based on data from 2010 [9,10]. The uptake for FOBT was 24.8% in people aged 40 to 60 years and that for OC in FOBT-positive people aged 40 to 60 years was 58.2%. Because no data were available for CTC screening, we assumed that half of the patients who were reluctant to undergo OC would agree to CTC screening and that all CTC-positive people would agree to OC.

##### *Strategy 1: Current program (without CTC), comparator*

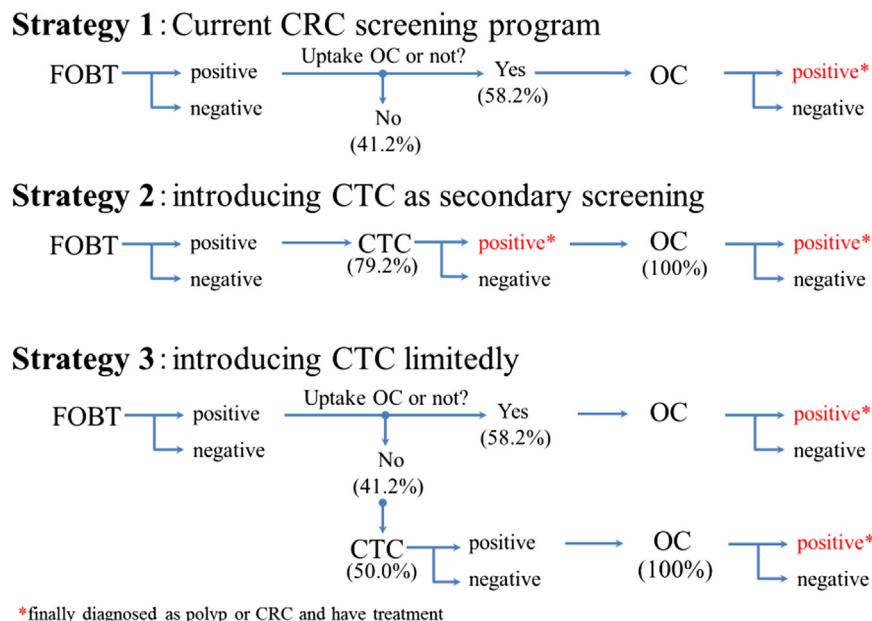
Strategy 1 reflected the current colorectal cancer screening program in Japan. FOBT was performed in those who were eligible for colorectal cancer screening (uptake 24.8%), and OC was performed in FOBT-positive persons who were willing to undergo OC (58.2%). CTC was not used.

##### *Strategy 2: Broad implementation of CTC*

FOBT was performed in those who are eligible for colorectal cancer screening (uptake 24.8%). CTC was performed in FOBT-positive persons who were willing to undergo CTC (79.1%). OC was performed in all CTC-positive persons (100%). Because 53.2% of the FOBT-positive persons were thought to be willing to undergo OC, we assumed that all of them were also willing to undergo CTC. Among the others (41.8%), we assumed that a half of them would undergo CTC. Therefore, the overall uptake of CTC was calculated to be  $58.2\% + (0.5 \times 41.8\%) = 79.1\%$ .

##### *Strategy 3: Limited implementation of CTC*

FOBT was performed in those who were eligible for colorectal cancer screening (uptake 24.8%). OC was performed in FOBT-positive persons who were willing to undergo OC (58.2%). In this strategy, unlike strategy 2, the candidates for CTC were not all FOBT-positive persons but only those who were FOBT-positive and also reluctant to undergo OC. We assumed that a half of



**Fig. 1 – Flowchart of three CRC screening strategies.** CRC, colorectal cancer; CTC, computed tomography colonography; FOBT, fecal occult blood test; OC, optical colonoscopy. \*Finally diagnosed as polyp or CRC and have treatment.

them would undergo CTC. Therefore, CTC was performed in 20.9% [ $0.5 \times (100 - 58.2\%)$ ] of all FOBT-positive people and OC was performed in all CTC-positive people (100%).

## Analysis

### Perspective

Analyses were carried out from a health care payer's perspective and included the costs of screening, polypectomy, and cancer treatment. FOBT costs were excluded from this study because they would be almost the same among all the three strategies.

### Target population

We analyzed a hypothetical cohort consisting of all those who were 40 years old on April 1, 2011. They were composed of 1,968,500 persons, which was estimated from the number of people aged 39 and 40 years in the public report about the population on October 1, 2010 [18].

### Model

We constructed a Markov model (Fig. 2) for colorectal cancer, with reference to previous studies [10–12], and adjusted it using the available epidemiological data from Japan [1–3,9,10] to estimate the effectiveness of CTC for colorectal cancer screening of working age population. One cycle of our Markov-model was set to 1 year, reflecting the shortest time period for data collected in our analysis [15,16,19].

### Transition probability

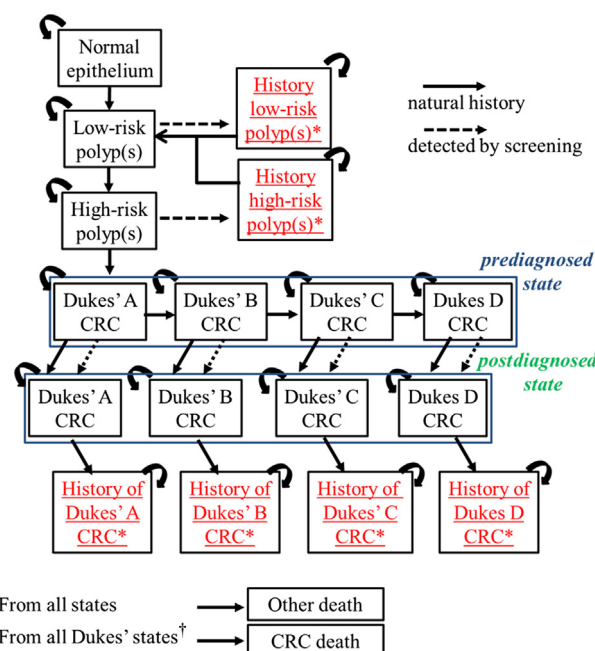
We adjusted the transition probabilities (Table 1) among each stage on the basis of epidemiological data from Japan [1–3,9,10] and a previous study [16]. Non-colorectal cancer mortality was calculated on the basis of colorectal cancer mortality [1] and mortality table [2].

We set the sensitivity and specificity of each test to the values presented in Table 1 on the basis of previous Japanese and foreign studies [20–27] and discussions with clinical experts.

Previous studies on the sensitivity and specificity of FOBT [20–26] have various limitations such as an insufficient sample size, a

biased population, or an insufficient description of the method. After discussion with clinical experts, we used the Japanese data [20] as provisional values in the base-case analysis and assumed distributions in the probabilistic sensitivity analysis.

Although the sensitivity and specificity of CTC depend largely on the skills of the physicians, we used the results of a clinical study [27] after assuming that interphysician variation had been equalized. Moreover, because there were few physicians in Japan



**Fig. 2 – Markov model for CRC [–].** CRC, colorectal cancer. \*Underline means already treated state. †Does not include the prediagnosed state.

**Table 1 – Valuables in the Markov model (transition probability, cost, and screening characteristics).**

Transition probability		Cost (JPY)		Other variables	
Progression (prediagnosed)		Test and treatment		Uptake rate of test	
Normal epithelium to low-risk polyp(s)	0.012	CTC*	31,500	FOBT <sup>†</sup>	0.248
Low-risk polyp(s) to high-risk polyp(s)	0.024	OC*	25,000	OC <sup>†</sup>	0.583
High-risk polyp(s) to Dukes' A	0.034	Polypectomy ( $\leq 2$ cm in diameter)	78,000	CTC	0.500
Dukes' A to Dukes' B	0.583	Polypectomy ( $\geq 2$ cm in diameter)	98,000	Sensitivity of FOBT	
Dukes' B to Dukes' C	0.656	Malignant tumor resection (colon)	840,400	Low-risk polyp	0.070
Dukes' C to Dukes' D	0.865	Malignant tumor resection (rectum)	1,130,900	High-risk polyp	0.200
Death from colorectal cancer		Postoperative chemotherapy	1,016,000	Dukes' A	0.538
Dukes' A <sup>‡</sup>	0.00545	Chemotherapy (Dukes' D, annual)	4,259,600	Dukes' B	0.700
Dukes' B <sup>‡</sup>	0.0282	Follow-up (Dukes' A and B)	35,600	Dukes' C and D	0.783
Dukes' C <sup>‡</sup>	0.0532	Follow-up (Dukes' C and D)	45,000	Sensitivity of CTC	
Dukes' D <sup>‡</sup>	0.310	Annual cost by stage		Low-risk polyp	0.650
Prediagnosed to postdiagnosed		Low-risk and high-risk polyps	78,000	Others	0.900
Dukes' A presentation	0.065	Dukes' A (1 y)	98,000	Sensitivity of OC	1.000
Dukes' B presentation	0.26	Dukes' A (2–5 y)	35,600	Specificity	
Dukes' C presentation	0.46	Dukes' B (1 y)	941,400	FOBT	0.948
Dukes' D presentation	0.92	Dukes' B (2–5 y)	35,600	CTC	0.860
Polyp recurrence after polypectomy		Dukes' C (1 y)	1,957,400	OC	1.000
History of low-risk polyp(s) (first year)	0.18	Dukes' C (2–5 y)	45,000		
History of low-risk polyp(s) (2 y)	0.05	Dukes' D (1–5 y)	4,304,600		
History of high-risk polyp(s) (first year)	0.25				
History of high-risk polyp(s) (2 y)	0.06				

CRC, colorectal cancer; CTC, computed tomography colonography; FOBT, fecal occult blood test; JPY, Japanese yen; OC, optical colonoscopy.

\* Derived from the fee for the cancer screening program at the National Cancer Center in Japan and others were calculated from the guideline for CRC treatment [30] and health insurance fee schedule [28,29].

<sup>†</sup> Average values among people aged 40 to 60 y appear in this table. In the actual model, they were varied according to their age [9,10].

<sup>‡</sup> Transition probabilities were adjusted by domestic epidemiological data [1–3,9,10] and the other probabilities were referred to a previous study [16].

who were experienced in CTC, the real-world sensitivity and specificity of CTC were likely to be lower than those published in this previous report [27]. We assumed distributions in the probabilistic sensitivity analysis to take account of this uncertainty.

Both the sensitivity and specificity of OC used in the final diagnosis were set to 1.00. If the specificity was below 1.00, some people would be false-positively diagnosed and unnecessarily treated for colorectal cancer. We did not, however, consider this issue in our model and did not perform any scenario analysis because there were insufficient Japanese epidemiological data about false-positive cases and the accuracy of OC itself was not in the scope of our analysis.

#### *Uptake of each test*

As mentioned earlier, we set the uptake of FOBT from the Comprehensive Survey of Living Conditions 2010 [9] and set the uptake of OC from the Report on Regional Public Health Services and Health Promotion Services 2010 [10]. Average uptake of FOBT and OC among people aged 40 to 60 years is presented in Table 1. Furthermore, scenario analysis was carried out for the case that the uptake of FOBT reached the government's target figure (50%) and the case that the uptake of OC was the lowest value (34.1% in Tokyo) or the highest value (75.0% in Iwate) among 47 prefectures [10].

Because colorectal cancer screening with CTC was not common in Japan, there were no national data about the uptake of CTC; therefore, from discussion with clinical experts, we assumed that a half of FOBT-positive persons who were reluctant to undergo OC would agree to CTC screening and that all CTC-positive people would agree to OC. The uptake of CTC is also presented in Table 1.

#### *Cost*

Costs are presented in Table 1 [28–30], all of which are direct costs. The costs of CTC and OC were based on those for cancer screening charged at the Japanese National Cancer Center. Treatment costs of colorectal cancer stratified by Dukes' classification were calculated from the newest guideline for colorectal cancer treatment [30]. Under the Japanese health insurance system, inpatient treatments for colorectal cancer in large hospitals were charged on the basis of the diagnosis-related group system. Thus, we used them instead of separately calculating unit price and resource use [28,29].

#### *Outcome measures*

We set QALY as the primary outcome and colorectal cancer death and expected life-years as secondary ones. Because there were insufficient Japanese data, we referred the utility scores in a previous UK study [15,16]. The Basic Plan to Promote Cancer Control Program aimed to decrease the number of cancer deaths and to prolong life-years with good health [7]. Thus, we set colorectal cancer death as well as expected life-year as secondary outcomes.

#### *Time horizon (duration of analyses)*

In the base-case analysis, the time horizon was set to 20 years. Governmental policy aimed at increasing the uptake of colorectal cancer screening, especially among those who were of working age [11]. Therefore, we think that 20 years was sufficient for capturing whole costs and outcomes accrued during the working age, or 40 years old to 60 years old. So far, some workers were still working even after they crossed 60 years, or until they become 65



years or 70 years old. Then, in scenario analyses, we varied the time horizon to 10 years, 30 years, and lifetime.

#### Discount rate

The annual discount rate was set at 3% for both cost and effectiveness. Scenario analysis was carried out for 0% and 7% in Shiroiwa et al. [31].

#### Sensitivity analyses

Scenario analyses were carried out for the following variables for which we could found the grounds of setting a lower or higher value: uptake of FOBT (50%) [7], uptake of CTC (25%–75%), uptake of OC (34.1% and 75.0%) [10], time horizon (10 years, 30 years, and lifetime), discount rate (0% and 7%) [31], and the cohort aged 50 years with a 10-year time horizon.

Probabilistic sensitivity analyses were also conducted by adopting distributions for variables incorporated into our model, as shown in Table 1. We adopted beta distributions for the parameters for which we could acquire raw data (denominator and numerator of parameters) and normal distributions for the parameters for which we could not acquire raw data. Also, we made estimations of the chemotherapy costs for Dukes' C and Dukes' D patients on the basis of chemotherapy strategies in the 2010 guideline [30] but there were various treatment modalities and it depends largely on the condition of the patient; therefore, we assumed the log-normal distribution for the chemotherapy cost on the basis of estimated costs distribution of each chemotherapy strategy, and considered uncertainties related to chemotherapy cost.

## Results

### Validity of the Model

We constructed a Markov model with reference to previous studies [15,16,19] and adjusted it for transition probability according to Japanese epidemiological data such as the 5-year observed survival rate, cumulative incidence rate, and cumulative mortality categorized by Dukes' classification [1–3,9,10]. For example, we calculated the annual mortality for each Dukes' classification from Japanese 5-year observed survival rate data. We adjusted the age-specific incidence of colorectal cancer using Japanese data for cumulative incidence rate and mortality. Because there

were no data for transition probabilities among the four Dukes' stages, we referred previous studies [15,16,19] and calibrated those using current data for the cumulative incidence rate.

### Result of the Base-Case Analysis

We calculated the total costs (screening cost + treatment costs), the QALYs, the number of colorectal cancer deaths, and the expected life-years for the hypothetical cohort consisting of all those who were 40 years old ( $N = 1,968,500$  as of April 1, 2011); the data are summarized in Table 2.

For the base-case analysis (time horizon 20 years), differences against strategy 1 were as follows.

Strategy 2 required an additional cost of JPY 3,790,548,000 (from 69,405,291,000 to 65,614,743,000), increased QALYs by 2,303 (from 28,158,349 to 28,156,046), decreased the number of cancer deaths by 324 people (from 4,693 to 4,369), and increased the expected life-years by 1,752 person-years (from 28,713,132 to 28,711,380). The incremental cost-effectiveness ratios (ICERs) were JPY 1,646,000 per QALY gained, JPY 11,683,000 per colorectal cancer death averted, and JPY 2,164,000 per life-year gained.

Strategy 3 decreased cost by JPY 1,736,198,000 (from 65,614,743,000 to 63,878,545,000), increased QALYs by 3,012 (from 28,159,058 to 28,156,046), decreased the number of cancer deaths by 434 people (from 4,693 to 4,260), and increased the expected life-years by 2,323 person-years (from 28,713,702 to 28,711,380). Strategy 3 was dominant against strategy 1.

### Result of scenario analyses

The scenario analyses were carried out for the following four variables: uptake of FOBT (50%), uptake of CTC (25%–75%), uptake of OC (34.1% and 75.0%), time horizon (10 years, 30 years, and lifetime), discount rate (0% and 7%), and the cohort aged 50 years with a 10-year time horizon.

When the uptake of FOBT reached the government's target figure (50%), the ICERs were JPY 2,795,000 per QALY gained for strategy 2 and JPY 154,000 per QALY gained for strategy 3, respectively, which was well below the Japanese threshold (JPY 5–6 million per QALY gained) [31].

When the uptake of CTC decreased from 50% to 25%, the ICER was JPY 6,175,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1. When the uptake of CTC improved from 50% to 75%, the ICER was JPY 850,000 per QALY gained for strategy 2 and strategy 3 was dominant against

**Table 2 – Result of base-case analysis (unit: 1,968,500 persons aged 40 y on April 1, 2011).**

Unit 1	Unit 2	Strategy 1*	Strategy 2	Strategy 3	Strategy 2 vs. strategy 1	Strategy 3 vs. strategy 1
Cost (JPY 1,000)	Cost	65,615,000	69,405,000	63,879,000		
	ΔCost				+3,790,548	–1,736,198
Outcome	QALY	28,158,046	28,158,349	28,159,058		
	CRC death	4,693	4,369	4,260		
	ELY	28,711,380	28,713,132	28,713,702		
	ΔQALY				2,303	3,012
	ΔCRC death				324	434
	ΔELY				1,752	2,323
ICER (JPY 1,000)	per QALY				1,646	Dominant
	per CRC death averted				11,683	Dominant
	per LYG				2,164	Dominant

CRC, colorectal cancer; ELY, expected life-year; ICER, incremental cost-effectiveness ratio; JPY, Japanese yen; LYG, life-year gained; QALY, quality-adjusted life-year.

\* Strategy 1 was set to control when calculating ICERs.

strategy 1.

When the uptake of OC decreased to the lowest value among 47 prefectures (34.1% in Tokyo), the ICER was JPY 21,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1. When the uptake of OC decreased to the highest value among 47 prefectures (75.0% in Iwate), the ICER was JPY 11,740,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1.

When the time horizon was 10 years, ICERs were JPY 19,085,000 per QALY gained for strategy 2 and JPY 5,288,000 per QALY gained for strategy 3, respectively. When the time horizon was 30 years, the ICER was JPY 416,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1. When the time horizon was lifetime, both strategy 2 and strategy 3 were dominant against strategy 1.

When the discount rate was 0%, the ICER was JPY 1,217,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1. When the discount rate was 7%, the ICER was JPY 2,401,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1.

When the target population was those who were aged 50 years on April 1, 2011, and the time horizon was 10 years, ICERs were JPY 2,685,000 per QALY gained for strategy 2 and JPY 5,468,000 per QALY gained for strategy 3 against strategy 1.

### Result of the Probabilistic Sensitivity Analysis

The probabilistic sensitivity analyses showed that colorectal cancer screening programs with CTC were likely to be cost-effective compared with strategy 1 (current program without CTC).

Figure 3 illustrates that in 95.2% of the simulations, strategy 2 was found to be acceptable at a cost-effective threshold of JPY 5 to 6 million per QALY gained compared with strategy 1. Moreover, Figure 3 shows that strategy 2 was dominant against strategy 1 in 6.1% of the simulations.

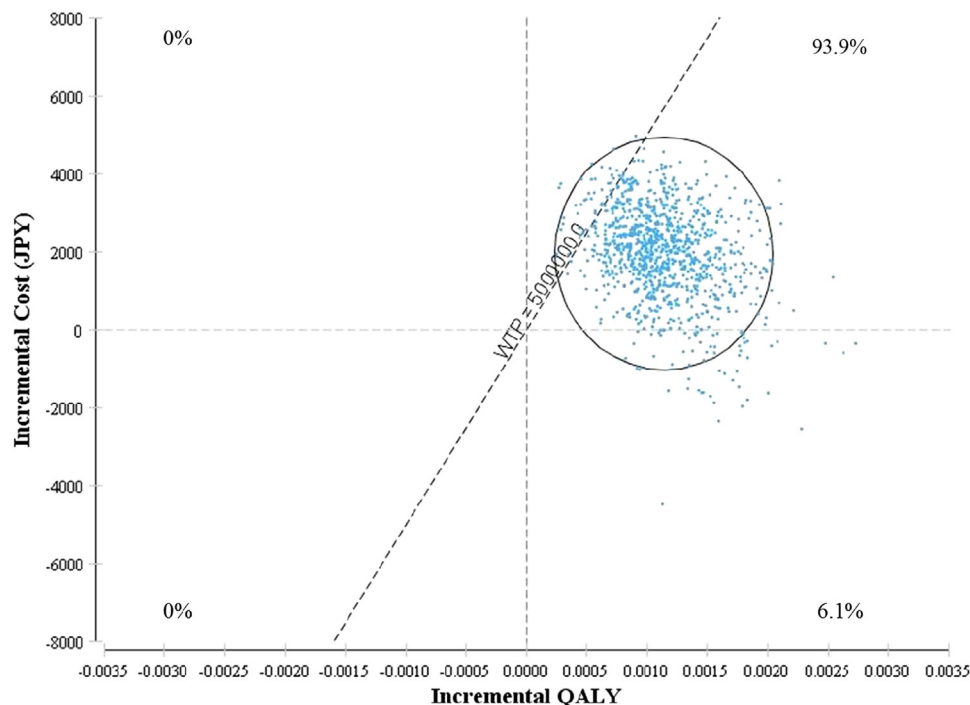


Fig. 3 – Scatter plot of probabilistic sensitivity analysis on the cost-effectiveness plane for strategy 2 compared with strategy 1. JPY, Japanese yen; QALY, quality-adjusted life-year; WTP, willingness to pay.

Figure 4 illustrates that in all simulations, strategy 3 was found to be acceptable at the cost threshold of JPY 5 to 6 million per QALY gained compared with strategy 1; moreover, Fig. 4 shows that strategy 3 was dominant against strategy 1 in 74.7% of the simulations.

## Discussion

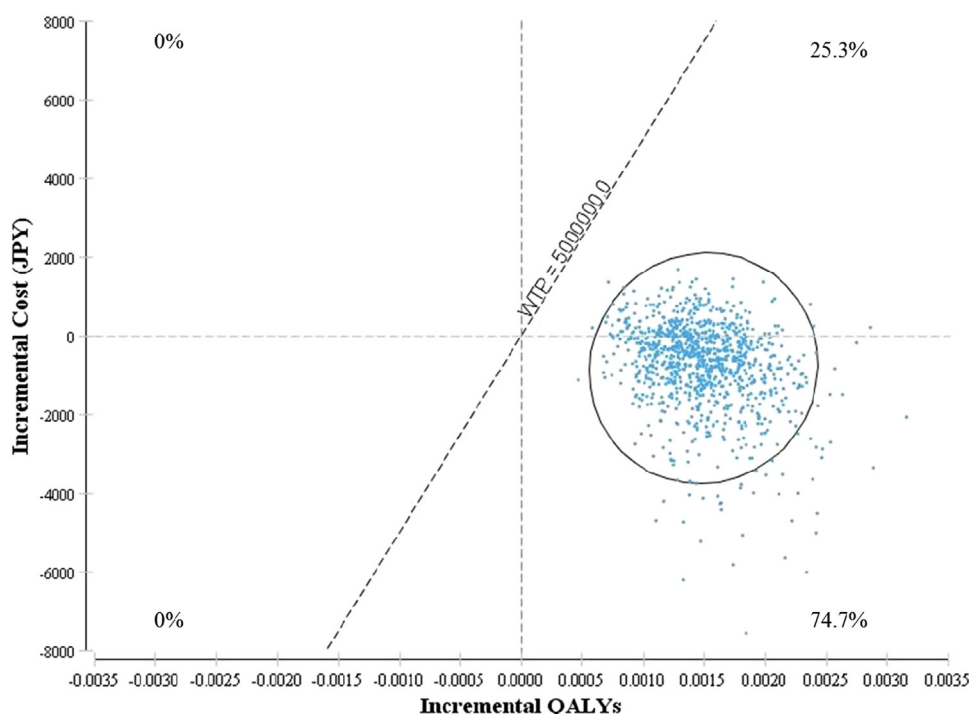
### Target Population

As mentioned earlier, since 2011, the Japanese government started to provide free colorectal cancer screening to those aged 40, 45, 50, 55, or 60 years, aiming to increase the colorectal cancer screening uptake to the target figure (50%) among the working age population [11]. Therefore, to reveal the effect of CTC for the colorectal cancer screening program among the working age population in Japan, we set a closed cohort comprising people aged 40 years on April 1, 2011, as our target population and set 20 years (from 40 to 60 years) as the time horizon in the base-case analysis.

The result of scenario analysis for time horizon showed the common trend between strategy 2 and strategy 3, that when the time horizon was longer, the cost-effectiveness of CTC for colorectal cancer screening would be improved more. Older persons, however, were more likely to be diagnosed with colorectal cancer when they took cancer screening, due to a higher prevalence rate than in younger people [3]. Therefore, to capture the entire effect of CTC implementation, we need to expand the time horizon to lifetime. If we expand the time horizon to lifetime, both strategy 2 and strategy 3 became dominant against strategy 1.

### Recurrence of Colorectal Cancer

We did not adapt recurrence and metastasis to this model, which was due to the lack of data on the recurrence of colorectal cancer in Japan. Their effect on mortality, however, could implicitly be reflected in the 5-year observed survival rate, while their cost had



**Fig. 4 – Scatter plot of probabilistic sensitivity analysis on the cost-effectiveness plane for strategy 3 compared with strategy 1. JPY, Japanese yen; QALY, quality-adjusted life-year; WTP, willingness to pay.**

not been calculated. Therefore, we might underestimate the per-patient treatment cost and the amount of cost saving generated by CTC, especially for colorectal cancer with Dukes' C and Dukes' D. If we could include the costs of recurrence and metastasis, the ICER would improve more.

### Limitations and Future Research

In this study, we constructed the model so that it worked adversely on introducing CTC where data were ambiguous, because colorectal cancer epidemiological data were not sufficient. It is desirable to perform a reanalysis with more data for the sensitivity and specificity of FOBT and a breakdown of the medical costs for each stage of the Dukes' classification.

However, we did not consider the adverse events that may occur with OC or CTC. Because OC was conducted by certified physicians who passed the training course in Japan, physicians in the National Cancer Center in Japan commented that adverse events such as perforation could be ignored in Japan. Also, radiologists commented that adverse events with CTC could be ignored because of small radiation exposure. Therefore, we ignored this issue in this model. But we had to take into account that the risk of adverse events with OC or CTC could not be zero. And, because this model ignores these risks, we should not forget this point when we use the result of this analysis. In any case, we would include these factors in future analyses to avoid this issue.

### Policy Consideration

Overall results were largely affected by the uptake of OC. Larger OC uptake induced better ICER and vice versa because of the number of those who took OC, and the number of people with colorectal cancer detected would be increased with higher OC uptake. OC uptake varied much from one region to another, or 34.1% to 75.0% [10]. Thus, we need to take regional OC uptake into account when we consider implementing and/or promoting CTC to a specific region.

### Conclusions

In our analysis, the cost-effectiveness of CTC for a colorectal cancer screening program in the working age population in Japan was as follows. The ICER was JPY 1,646,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1, both of which were well below the Japanese threshold (JPY 5–6 million per QALY gained) [31].

These ICER values will be further improved with a longer time horizon (i.e., 30 years) than used in the basic analysis. Therefore, adding CTC into the current colorectal cancer screening program for the working age population seems to be a cost-effective option.

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